

### REMARKS

The Examiner rejected claims 25-54. Claims 25, 27, 28, 33, 35, 36, and 38 are amended herein, and claims 41-54 have been canceled without prejudice. Thus, claims 25-40 are pending. Specifically, claim 25 has been amended to recite a polypeptide consisting essentially of a self IgE CH3 domain and one or more non-self IgE domains, wherein at least one of the non-self IgE domains comprises an IgE sequence present in a non-placental mammal. Claim 27 has been amended to recite that the sequence of the immunogenic polypeptide is as set forth in SEQ ID NO:4, and claim 28 has been amended to depend from claim 25. Similarly, claim 33 has been amended to recite an immunogenic polypeptide consisting essentially of one or more non-self IgE domains and at least an N-terminal half of a self IgE CH3 domain, wherein at least one of the non-self IgE domains comprises an IgE sequence present in a non-placental mammal. Claim 35 has been amended to recite that the sequence of the immunogenic polypeptide is as set forth in SEQ ID NO:4, and claim 36 has been amended to depend from claim 33. Claim 38 has been amended for consistency with claim 33. Support for these amendments can be found throughout the specification. For example, Figure 2 discloses immunogenic polypeptides consisting essentially of CH3 domains in combination with CH2 and CH4 domains of non-placental mammals. In addition, original claims 27 and 35 disclose that at least one of the non-self IgE domains can contain an IgE sequence present in a non-placental mammal. The specification has been amended to add sequence identifiers to the Description of Drawings. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicant respectfully requests reconsideration and allowance of claims 25-40.

### Examiner Interviews

Applicant's agent thanks Examiner Huynh for the courtesy of the telephonic interview on November 12, 2002. Applicant's agent also thanks Examiner Huynh and Primary Examiner Chan for the courtesy of the telephonic interview on December 18, 2002. The substance of these telephonic interviews involved the issues and arguments presented herein.

### Objections

The Examiner objected to the disclosure for the following informalities: (1) SEQ ID NOs are required in the Description of the Drawings for Figures 1 and 2; (2) the Description of Drawings for Figures 2A and 2B does not correspond to the submitted figures; and (3) Figure 3A was missing from the formal drawings filed on April 19, 2002.

Applicant has amended the specification to insert sequence identifiers into the Description of Drawings for Figures 1 and 2. With respect to Figure 2A, Applicant submits that "Fig 2a1" and "Fig 2a2" are the first and second pages of Figure 2A, respectfully, while "Fig 2a" is an illustration for the draftsman as to how the two pages should be assembled. Similarly, "Fig 2b1" and "Fig 2b2" are the first and second pages of Figure 2B, respectfully, and "Fig 2b" is an illustration as to how the two pages should be assembled. Figure 3A is resubmitted herewith.

The Examiner also objected to claims 53 and 54 because they depend on non-existing claim 58. Applicant has canceled claims 53 and 54. Thus, this objection is moot.

### Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 25-54 under 35 U.S.C. § 112, first paragraph, as being based on a disclosure that is not enabling. The Examiner stated:

... the specification, while being enabling only for immunogenic polypeptides such as the ones shown in Fig 2 consisting of a self IgE CH3 domain from rat, human, mouse, dog or pig and one or more non-self IgE domains such as an IgE CH2 domain from opossum or platypus and an IgE CH4 domain from opossum or wombat to induce an anti-self IgE response in a mammal, "does not reasonably provide enablement for (1) *any* immunogenic polypeptide comprising a self IgE CH3 domain and one or more non-self IgE domains, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response on a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein at least one of said non-self IgE domains "comprises" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby, and (2) *any* immunogenic polypeptide comprising a self IgE domain and one or more non-self IgE domains wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal and wherein said at least one non-self IgE domains "comprises" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby.

See, OA at pp. 2-3. The Examiner further stated that the specification does not enable a person of skill in the art to make and use the invention commensurate in scope with the claims.

The Examiner also asserted that "the specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation." In particular, the Examiner cited the following factors from *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)): the scope of the claims, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art, and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The Examiner also stated that the specification discloses only immunogenic polypeptides such as those shown in Figure 2, and that the specification does not teach how to make and use *any* immunogenic polypeptide in which at least one of the non-self IgE domains "comprises" an IgE sequence from *any* "non-placental mammal." With respect to use of the open-ended term "comprises," the Examiner asserted that the specification does not provide guidance "as to what type and number of amino acids can be added and whether after addition of amino acids that the immunogenic polypeptide would retain both structure and function such as stabilizes the functional conformation of the self-IgE CH3 domain since the CH3 domain is critical for IgE binding to the high affinity FcεRI." See, OA at p. 3. In addition, the Examiner stated:

Given the indefinite number of undisclosed immunogenic polypeptides comprising a self IgE CH3 domain and *any* one or more non-self IgE domains, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein at least one of said non-self IgE domains "comprises" *any* IgE sequence present in *any* undisclosed "non-placental mammal" such as koala, kangaroo, and wallaby, it is unpredictable which undisclosed immunogenic polypeptide would be useful for inducing an anti-self response in a mammal.

See, OA at p. 4.

Applicant respectfully disagrees. A person having ordinary skill in the art at the time the application was filed reading Applicant's specification would have been able to make and use the originally claimed polypeptides without undue experimentation. For example, a person having ordinary skill in the art would have been able to make a polypeptide containing both an IgE CH3 domain from a particular mammal (a self IgE CH3 domain) and one or more IgE domains from any other mammal (non-self IgE domains). In fact, a person having ordinary skill in the art at the time the application was filed in 1998 would have been able to obtain IgE sequences from any species using routine methods such as PCR or library screening techniques. In addition, a

person having ordinary skill in the art would have been able to add any amino acid sequence to the immunogenic polypeptide. In fact, as disclosed in the specification, for example, sequences such as a signal sequence, a His tag sequence, and/or cytokine sequences (e.g., interferon- $\alpha$ , interferon- $\beta$ , interferon- $\gamma$ , TNF- $\alpha$ , IL-1, IL-2, IL-4, IL-6, IL-12, IL-15, IL-18, or granulocyte-macrophage colony stimulating factor sequences) can be added to the immunogenic polypeptides without undue experimentation. See, e.g., Applicant's specification at page 11, lines 7-9 and lines 28-29; page 15, line 15 through page 17, line 6; and page 23, lines 3-7.

To further prosecution, however, claim 25 has been amended to recite that the polypeptide consists essentially of a self IgE CH3 domain and one or more non-self IgE domains. Claim 25 also requires at least one of the non-self IgE domains to contain an IgE sequence present in a non-placental mammal. In addition, claim 33 has been amended to recite that the polypeptide consists essentially of one or more non-self IgE domains and at least an N-terminal half of a self IgE CH3 domain. Claim 33 also requires at least one of the non-self IgE domains to contain an IgE sequence present in a non-placental mammal. A person having ordinary skill in the art at the time the application was filed reading Applicant's specification would have been able to make and use immunogenic polypeptides consisting essentially of (1) a self IgE CH3 domain or at least an N-terminal half thereof and (2) one or more non-self IgE domains without undue experimentation. Thus, Applicant's specification fully enables the presently claimed invention.

In light of the above, Applicant respectfully requests withdrawal of this rejection of claims 25-40 under 35 U.S.C. § 112, first paragraph.

The Examiner also rejected claims 25-54 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. Specifically, the Examiner stated:

... the specification does not reasonably provide a written description of (1) *any* immunogenic polypeptide, comprising a self IgE CH3 domain and one or more non-self IgE domains, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE wherein at least one of said non-self IgE domains "comprises" an IgE sequence present

in *any* "non-placental mammal" such as koala, kangaroo, and wallaby, and (2) *any* immunogenic polypeptide comprising a self IgE domain and one or more non-self IgE domains wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal and wherein said at least one non-self IgE domain "comprises" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby.

See, OA at pp. 4-5. The Examiner further stated that with the exception of the specific immunogenic polypeptides such as those shown in Figure 2, "there is insufficient written description about the structure associated with function of *any* immunogenic polypeptide comprising a self IgE CH3 domain and *any* one or more non-self IgE domains "comprising" an IgE sequence present in *any* "non-placental mammal" such as koala, kangaroo, and wallaby" (see, OA at p. 5). In addition, the Examiner asserted that since the specification discloses non-self IgE domains from "only" three species of non-placental mammals, "one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus" (OA at p. 5), and thus Applicant was not in possession of the claimed genus.

Applicant respectfully disagrees. The written description requirement does not require all members of a genus to be described within a patent application, but rather that "a representative number of species" be described. A "representative number of species" is defined as meaning that the species that are adequately described are representative of the genus. See, MPEP § 2163(a)(ii). A person having ordinary skill in the art would have appreciated that Applicant's specification adequately describes the originally claimed invention.

To further prosecution, however, independent claims 25 and 33 have been amended by replacing the term "comprising" with the term "consisting essentially of," and claims 41-54 have been canceled. A person having ordinary skill in the art would have appreciated that Applicant's specification adequately describes immunogenic polypeptides consisting essentially of (1) a self IgE CH3 domain or at least an N-terminal half thereof and (2) one or more non-self IgE domains. This is particularly true given the multiple examples of immunogenic polypeptides disclosed, for example, in Figure 2 of Applicant's specification. Thus, the immunogenic polypeptides recited in the present claims are fully described in Applicant's specification.

In light of the above, Applicant respectfully requests withdrawal of this rejection of claims 25-40 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 48-49 and 52-54 under 35 U.S.C. § 102(b) as being anticipated by Nissim *et al.* (*EMBO J.*, 10(1):101-107, 1991). The Examiner stated that the Nissim *et al.* reference teaches a polypeptide containing a self mouse IgE CH3 domain and one or more non-self IgE domains such as human IgE CH1, CH2, and CH4 domains, wherein the reference polypeptide lacks a light chain Ig sequence.

Applicant respectfully disagrees. The originally claimed polypeptides are not anticipated by Nissim *et al.* To further prosecution, however, claims 48-49 and 52-54 have been canceled. Thus, this rejection is moot.

The Examiner also rejected claims 25-26, 29, 31, 48-49, and 53 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,653,980 (the '980 patent). Specifically, the Examiner stated that the '980 patent teaches "a polypeptide comprising the amino acid sequence (the entire sequence or part thereof) of the constant CH2-CH3 domains of IgE that lacks the CH1 domain from mammalian species such as human and rat wherein the reference IgE domains are mutated by exchange (self versus non-self) fused to glutathione-S-transferase (Sj26) from *S. japonicum* (See column 4, lines 21-26, column 9, lines 22-26, in particular)." See, OA at p. 6.

Applicant respectfully disagrees. The '980 patent does not anticipate the originally claimed immunogenic polypeptides. In addition, the '980 patent does not anticipate claim 25 as amended. The '980 patent discloses a vaccine containing a protein having the amino acid sequence (the entire sequence or a part thereof) of the constant CH2-CH3 domains of the epsilon chain of the IgE molecule. Nowhere does the '980 patent teach or suggest making a polypeptide having a self IgE CH3 domain and one or more non-self IgE domains, let alone an immunogenic polypeptide having one or more non-self IgE domains wherein at least one of the non-self IgE domains contains an IgE sequence present in a non-placental mammal. In fact, the '980 patent contains no language to indicate that self and non-self IgE sequences can be exchanged. The portions of the '980 patent cited by the Examiner simply disclose that the polypeptide can contain mutations such as amino acid substitutions. This falls far short of suggesting that a person having ordinary skill in the art should combine self and non-self IgE domains to arrive at

the presently claimed immunogenic polypeptides. Thus, the present claims are not anticipated by the '980 patent.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 25-26, 29, and 31 under 35 U.S.C. § 102(b) over the '980 patent.

#### Rejections under 35 U.S.C. § 103

The Examiner rejected claims 33-34 and 37-39 under 35 U.S.C. § 103(a) as being unpatentable over the '980 patent. The Examiner stated that the claimed invention as recited in claim 33 differs from the '980 patent only in that the claimed polypeptide includes the N-terminal half of a self IgE CH3 domain, wherein the polypeptide is effective to induce an anti-self response in a mammal. The Examiner further stated that the '980 patent teaches that there is a risk that the C-terminal part of the CH3 domain may give rise to anaphylactic shock in the mammals in which the antibodies are formed, and that it would have been obvious to one of ordinary skill in the art at the time the invention was made to exclude the C-terminal part of the CH3 domain as taught by the '980 patent. In addition, the Examiner asserted that one of ordinary skill in the art at the time the invention was made would have been motivated to exclude the C-terminal part of the CH3 domain because of the teaching of the '980 patent.

Applicant respectfully disagrees. The '980 patent does not render original claim 33 obvious. In addition, the '980 patent does not render amended claim 33 obvious. Nowhere does the '980 patent teach or suggest making an immunogenic polypeptide consisting essentially of at least an N-terminal half of a self IgE CH3 domain and one or more non-self IgE domains, let alone an immunogenic polypeptide with a non-self IgE domain having a sequence present in a non-placental mammal. As such, the '980 patent does not render amended claim 33 obvious.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 33-34 and 37-39 under 35 U.S.C. § 103(a) over the '980 patent.

The Examiner also rejected claims 27-28, 35-36, 41, 43, and 50-51 under 35 U.S.C. § 103(a) as being unpatentable over Nissim *et al.* or the '980 patent. Specifically, the Examiner stated that the invention as recited in claims 27, 35, 41, and 50 differs from the references only in that at least one of the non-self IgE domains contains an IgE sequence from a non-placental

mammal. The Examiner also stated that the invention as recited in claims 28, 36, 43, and 51 differs from the references only in that the non-placental mammal is selected from the group consisting of opossum, platypus, and wombat. The Examiner further asserted that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the non-self IgE domains from placental mammals as taught by Nissim *et al.* or the '980 patent for IgE domains from the most evolutionarily distantly related non-placental mammals, and that a person of ordinary skill in the art would have been motivated to do so "because non-placental mammals are the most distantly related mammals to placental mammals." See, OA at p. 8.

Applicant respectfully disagrees. Neither Nissim *et al.* nor the '980 patent renders original claims 27-28, 35-36, 41, 43, or 50-51 obvious. In addition, neither cited reference renders the amended claims obvious. In fact, at no point do the cited references suggest making an immunogenic polypeptide that (1) consists essentially of a self IgE CH3 domain and one or more non-self IgE domains, wherein at least one of the non-self IgE domains contains an IgE sequence present in a non-placental mammal, and (2) lacks a CH1 domain of IgE. Likewise, at no point do the cited references suggest making an immunogenic polypeptide that consists essentially of one or more non-self IgE domains and at least an N-terminal half of a self IgE CH3 domain, wherein at least one of the non-self IgE domains contains an IgE sequence present in a non-placental mammal. Moreover, the cited references do not suggest substituting non-self IgE domains from placental mammals with non-self IgE domains from non-placental mammals. In fact, a person having ordinary skill in the art reading the cited references would not have been motivated to substitute any non-placental mammalian IgE sequence for the IgE sequences disclosed in the cited references. The mere existence of evolutionary distance between non-placental and placental mammals suggests nothing about the desirability of substituting their IgE domains. Given these deficiencies, the cited references fail to render the present invention obvious.

In light of the above, Applicant respectfully requests withdrawal of the rejection of claims 27-28 and 35-36 under 35 U.S.C. § 103(a) over Nissim *et al.* or the '980 patent.

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### CONCLUSION

Attached is a marked-up version of the changes being made by the current amendments. Applicant submits that claims 25-40 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. Enclosed is a check for the Petition for Extension of Time fee. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

Date: January 2, 2003

  
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**Version with markings to show changes made**

**In the specification:**

The paragraph beginning at page 7, line 26, has been amended as follows:

Figure 1 is a diagram comparing the amino acid sequences of the CH2-CH3-CH4 domains of human (SEQ ID NO:1), rat (SEQ ID NO:2), and opossum IgE (SEQ ID NO:3), in the upper, middle, and lower rows, respectively. The opossum sequence also contains an N-terminal signal sequence followed by six histidine residues.

The paragraph beginning at page 7, line 30, has been amended as follows:

Figures 2A-B contain diagrams comparing the amino acid sequences of various polypeptides containing the following components: opossum CH2—rat CH3—opossum CH4 (ORO) (SEQ ID NO:4); opossum CH2—rat N-term CH3—opossum C-term CH3—opossum CH4 (ORO-trunc) (SEQ ID NO:5); opossum CH2—mouse CH3—opossum CH4 (OMO) (SEQ ID NO:6); opossum CH2—CH3—CH4 (OOO) (SEQ ID NO:3); platypus CH2—CH3—CH4 (PPP) (SEQ ID NO:7); opossum CH2—human CH3—opossum CH4 (OHO) (SEQ ID NO:8); opossum CH2—pig CH3—opossum CH4 (OPO) (SEQ ID NO:9); and opossum CH2—dog CH3—opossum CH4 (ODO) (SEQ ID NO:10). The arrows indicate domain borders.

**In the claims:**

Claims 41-54 have been canceled.

Claims 25, 27, 28, 33, 35, 36, and 38 have been amended as follows:

25. (Amended Twice) An immunogenic polypeptide, [comprising] consisting essentially of a self IgE CH3 domain and one or more non-self IgE domains, wherein at least one of said non-self IgE domains comprises an IgE sequence present in a non-placental mammal, wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal, and wherein said immunogenic polypeptide lacks a CH1 domain of IgE.

27. (Amended Twice) The immunogenic polypeptide of claim 26, wherein [at least one of said non-self IgE domains comprises an IgE sequence present in a non-placental mammal] the sequence of said immunogenic polypeptide is as set forth in SEQ ID NO:4.

28. (Amended Once) The immunogenic polypeptide of claim [27] 25, wherein said non-placental mammal is selected from the group consisting of opossum, platypus, koala, kangaroo, wallaby, and wombat.

33. (Amended Twice) An immunogenic polypeptide, [comprising] consisting essentially of one or more non-self IgE domains, and at least an N-terminal half of a self IgE CH3 domain, wherein at least one of said non-self IgE domains comprises an IgE sequence present in a non-placental mammal, and wherein said immunogenic polypeptide is effective to induce an anti-self IgE response in a mammal.

35. (Amended Twice) The immunogenic polypeptide of claim 34, wherein [at least one of said non-self IgE domains comprises an IgE sequence present in a non-placental mammal] the sequence of said immunogenic polypeptide is as set forth in SEQ ID NO:4.

36. (Amended Once) The immunogenic polypeptide of claim [35] 33, wherein said non-placental mammal is selected from the group consisting of opossum, platypus, koala, kangaroo, wallaby, and wombat.

38. (Amended Twice) The immunogenic polypeptide of claim 33, wherein one of said non-self IgE domains is an IgE CH2 domain, wherein one of said non-self IgE domains is an IgE CH4 domain, and wherein said at least an N-terminal half of a self IgE CH3 domain is located between said IgE CH2 domain and said IgE CH4 domain.